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ORTHOGENESIS AND SEROLOGICAL PHENOMENA

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As my discussion progresses I fear that some of my hearers may be reminded of the old joke about the mongoose. A stranger carrying an odd-looking box was asked by a man whose curiosity got the better of his good manners, what was in the box. The stranger replied that it was a mongoose and went on to explain that his brother was subject to delirium tremens, during the attacks of which he believed that he was being strangled by snakes; this mongoose was to catch the snakes. To the reminder by the inquisitive man that these were imaginary snakes he retorted, ' ' Yes, I know, but this is an imaginary mongoose.' '

Since some of our most competent investigators in the fields of genetics and evolution are skeptical apparently about the whole question of orthogenesis, to them, at least, I shall be making an imaginary attack upon a mythical phenomenon. President Kofoid, however, seemed to think that some of the recent work with immune sera done in my laboratory, which strongly indicates the induction of permanent germinal modifications, might have possible theoretical implications bearing on the question of orthogenesis, and I agreed to discuss the subject, although realizing at the outset that the net result would not be a scientific proof, but merely a suggestion which might possibly be of some value as one of various working hypotheses.

First as to orthogenesis itself; is there such a process? Our answer must depend largely upon how we define orthogenesis. It takes but a glance at the literature of the subject to see that it has meant many different things to many different people, ranging from a mystical inner perfecting principle, to merely a general trend in development due to the natural constitutional restrictions of the germinal materials, or to the physical limitations imposed by a narrow environment. In most modern statements of the theory, the idea of continuous and progressive change in one or more characters, due according to some to internal factors, according to others to external causes—evolution in a "straight line"—seems to be the central idea. To many, faced by the seeming impossibility of explaining by natural selection the origins of new characters, it has been apparently merely a welcome general utility concept by which one may account for the beginnings of new organs, or the development of parts along definite lines, irrespective of utility.

For present purposes nothing is to be gained by a review of the different theories of orthogenesis, all so well summarized in Kellogg's "Darwinism To-day," and I shall proceed merely on the assumption that, judging from the statistical law of errors, certain variations are apparently not fortuitous, since they tend to accumulate in certain directions. It is customary to add that the lines of development which result are independent of, and in extreme cases may be opposed to, the operation of natural selection. I see no reason, however, for believing that if variations occur in definite directions of no use to the organism, why they may not also occur just as definitely in directions which lend themselves to the perfecting influences of natural selection. The difficulty in determining this point lies in the fact that an evolution based on the selection of even fortuitous variations must in one sense be orthogenetic, that is, along definite lines, so that there is no way in retrospect of telling whether the underlying germinal variations were purely fortuitous, or whether they were biased toward an adaptive outcome.

Of the various lines of evidence brought forward in support of theories of orthogenesis, the ones which appeal most convincingly to me are: (1) those based on parallelisms in variation which appear in different branches of the same large group of organisms; (2) those argued from the premise that the very nature of the chemical complexes which constitute the body of a living organism necessarily limit changes to relatively few directions; and (3) some of those instanced in the field of palæontology.

As to examples of parallelisms in related forms, I am most familiar with conditions to be seen in the color patterns of the pheasants (*Phasianinæ*) and the guineas (*Numidinæ*). In a paper[1] written some years ago I summarized my observation on various features of the coloration in a number of groups of genera and species in these two subfamilies as follows:

> . . . there are certain basic tendencies for particular elements of the coloration, such as the formation of eye-spots, barring, and the like, to follow along definite paths of development. When arranged with reference to one of these elements, such, for example, as barring, which is one of the most universal, instead of possessing distinct and unrelated markings, the different species in a given group are seen to be standing merely at different levels in the development of one, or at most a few, continuous progressions of the special pattern in question. Since when so grouped the gradation in pattern is as much in evidence between collateral kinsmen as between those of direct lineage, one can only conclude that the bias toward a particular line of patterns is the product of fundamental protoplasmic peculiarities implanted in the group as a whole.

Further on in the same paper it is shown that where the pattern has become obscured it may be brought to expression again through hybridization. In the interesting group known as the peacock pheasants (*Polyplectron*) which by systematists is regarded as intermediate between the peafowls and the pheasants in the narrower sense, the varying stages and types of ocellation to be seen afford a good illustration of the point at issue. Quoting again from this earlier study:

> Again as regards ocelli or "eye-spots" in *P. chalcurus*, which appears to be the most generalized species, one finds no ocellation. The only hint of what is to be realized in the more specialized

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[1] *Jour. Exp. Zool.*, VII, 4, 1909.

members of the group is found in a pronounced purplish and greenish "metallic" coloration present on certain feathers of the tail. In the male of *P. emphanes,* while there are numerous green metallic iridescent areas on the feathers of the upper wings and back, they have not yet progressed to the condition of being definite ocelli, although on the tail of this same individual there are two transverse bands (the one on the retrices, the other on the upper tail coverts) of ocelli. Still a step in advance, in the male of *P. thibetanum,* Gm. (*P. alboocellatum* Cuv.; type, Mus. d'hist. nat., Paris) the small feathers of the wings and the feathers of the inter-scapular region bear distinct small purple ocelli ringed successively with black, light brown, and white. The tail is also banded with ocelli. In the male of *P. germaini* the wing-coverts and back bear numerous green ocelli. The female of this species, as usual less advanced phylogenetically than the male, has the ocelli of the body much less distinctly marked.

An idea frequently attached to the theory of ortho genesis, yet which I believe is in no wise a necessary part of it, is that the various grades of a feature supposed to show orthogenesis have arisen as a connected succession, the supposedly most advanced stage having emerged from the stage next in order below it. That the individuals of a large group which show some particular characteristic expressed in different degree can be arranged in a gradational series with reference to that characteristic is obvious, but, as pointed out by various critics of the theory, this does not prove that the various expressions of the character in question arose thus sequentially. In a recent study yet unpublished, made by Miss Sarah V. Jones in the department of genetics at the University of Wisconsin, on the genetical behavior of checks and bars in inheritance in pigeons, for example, Miss Jones corroborates the results obtained by Staples-Browne and by Bonhote and Smalley which show that the two patterns are independently inherited in Mendelian fashion with checked-wing dominant to barred. She also found the relation of uniform black to check to be one of simple dominance, and furthermore, that certain grades of checking are inherited independently. But she found no evidence in support of the well-known view of Whitman that the various grades of checks form a series moving in one direction, the ultimate outcome of which is the two-barred and finally barless types. And Miss Jones points out that it does not "necessarily follow that because the interaction of these several factors produces an apparent epistatic series, the mutations producing the various grades of checking should have occurred in any particular order."

And here, to my mind, is the crux of the matter. In order to have what may legitimately be termed orthogenesis, do the underlying mutations have to occur in any particular order? Is not the very fact that, instead of existing as a medley of wholly unrelated elements, certain characteristics of organisms, such as color markings, can frequently be arranged as parts of a definite pattern or as stages in a general process—does not this in itself indicate directional variation? When one sees in its incipiency, as it were, in one species a character which has attained to an advanced expression in a kindred group, especially where there are intermediate expressions of the same characteristic in other related species, is not this indicative of a general trend in variation? For instance, is not the tendency toward the formation of "eye-spots" in the plumage of the pheasants hinted at even in the greenish-black iridescence so often visible in the tail feathers of the common rooster—is not this tendency the expression of what in last analysis must be a germinal bias? To be sure, this bias finds different ranges of expression in different species: as eye-spots on the wing-feathers in some species, on the body-feathers in others. In one species they may occur as a single row of ocelli, in another as two rows, across the tail. And it is obvious that certain of these patterns have not been derived directly from others, since they appear in what are clearly collateral lines. Nevertheless, the tendency to form ocellations is present in many if not all species of this great group. We know nothing of the order in which the mutations occurred which brought about any particular condition that at present exists in the group. Some of them may have been small and sequentially related, and it is not impossible that the extremes were thrown in one line, while grades of less advanced type came into expression in collateral lines. It is also clear that even should certain grades have arisen as a progressive series there is no reason, from the viewpoint of the mutation theory, why any two particular grades should not show the characteristics of Mendelian unit-characters, irrespective of the order of their origin. The important point is that in this group when mutations occur in certain color pattern-controlling factors, whether great or small, they tend toward the formation of eye-spots in some degree.

While we know little of the chemistry of animal pigments, the reactions involved in color-production in certain plants are better understood, since many of the pigments have been extracted and analyzed. Along with the understanding of structure that has been gained in the chemical studies of synthetic dye-stuffs, has come considerable knowledge of the relation between color and molecular structure. In many cases, for instance, as Nietzki[2] has shown, where the pigments of most simple construction are yellow, by increase of molecular weight they change to red, next to violet, then to blue. A good review of the theories of color in organic compounds, given as an introduction to her own painstaking and valuable chemical researches[2] on "Pigments of Flowering Plants," will be found in a recent paper by Dr. Nellie A. Wakeman. Most of the information about organic pigments used in the present discussion has been obtained from this source.

Upon reading such a piece of investigation together with the accompanying discussion of related studies one is impressed by the fact that a comparatively few processes underlie most pigmentary changes in plants. Enzymes—hydrolases, reductases and oxidases—frequently play an important part in the formation of pigments, or in changes in pigments already formed. Shade of color, for example, is evidently often merely a function of oxidase content. With a graded increase of oxidase, therefore, a plant might be put through a regular gamut of color effects. In general, the mere addition of hydrogen to dye-stuffs reduces them to the corresponding leuco base. Armstrong, in his quinone theory of color, makes much of the quinones as the colored compounds in dye-stuffs and maintains that the corresponding colorless compounds are hydro-quinones. The structure and size of the pigment molecule itself seems to be an important factor in color. Hydrocarbon radicals, for instance, deepen the tint; the addition of hydrogen raises the tint. In analyzing any particular case one has to take into account the original molecule, the position of any group introduced and the number of groups introduced. It is possible, for example, by the introduction of a tint-deepening group to deepen the color, but by introducing two or three more such groups to throw the absorption wholly outside the visible spectrum and thus do away with the color. From this it is clear that two compounds may be closely related in constitution and yet one be colored, the other colorless. As to why, physically, in both the aromatic and the aliphatic series, color is produced in certain compounds and not in others, various investigators have arrived at the conclusion that the cause of color is due to "the making and breaking of contact between atoms, thus giving them marked activity," a process known as *isorropesis,* and Miss Wakeman goes on to explain:

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[2] *Trans. Wis. Acad.*, XIX, Part II, pp. 767–906, Madison, Wis.

> This change of linkage which must accompany the transformation of one modification of the compound to the other is the source of the oscillations producing the absorption bands. If these oscillations are synchronous with light waves of a high frequency they give rise to absorption bands in the ultra violet and the compound is colorless. If, however, they are less frequent, the absorption band appears in the visible portion of the spectrum and this absorption of colored rays results in the compound taking on complementary color.

Among interesting facts that come to light in Miss Wakeman's summarization may be mentioned the following: all organic pigment molecules are unsaturated; the quinone grouping is one of the best known of the chromophorous groups; by far the largest number of plant pigments are referable to hydrocarbons of saturation C_nH_{2n-14} and C_nH_{2n-16}; and finally, that it is the relation of the chromophorous groups to each other and to the rest of the molecule, and not their mere presence in the molecule, that postulates color in a substance.

I may seem to have dwelt unduly upon pigmentation in plants but I have tried to go into the matter only sufficiently to give a glimpse of some of the real conditions which underlie some of the "unit-characters" we are juggling about in genetics, and around which we are attempting to frame hypotheses of evolution. Color, perhaps more than any other one thing, has in recent years been utilized for genetical observations. And when it is known that in many cases color is merely a function of the degree of oxidation of some fundamental compound, or the introduction or subtraction of some hydrocarbon radical, it does not tax the imagination to conceive of how it is possible to have series of color "characters" that in the parlance of organic evolution represent orthogenetic series. As simple a matter as the relative degree of oxygen supply, probably determined by the amount of an oxidase present, may account for various stages of color. It is manifest, moreover, that in a given group there might easily be a tendency toward increase in oxidase-production, which if present unequally in different collateral lines might give us just the uneven condition, with different species standing at different levels of expression of the trait in question, which exists in various alleged cases of orthogenesis. It is obvious, furthermore, that any higher state of development of the character in a particular species need not have sprung from the next lower stage, but may have had its immediate origin from any level of the scale.

Most of the constitutional changes which go on in the living organism seem to center in the proteins of the protoplasm. Metabolism is largely a question of the disruption and reconstruction of the various cell-proteins. In the cell, moreover, the characteristic protein-complexes themselves determine the nature of the synthesis that shall go on. When synthetic activity is more than sufficient to make good metabolic waste, growth results, and when such increase becomes overgrowth and takes the form of a detached individual, we pronounce it reproduction. We are then in position to talk about inheritance—the fact that a new individual possesses the properties and, under similar conditions, therefore, will express the activities and take on the appearances of the earlier or parent form. Thus the germ-cell is a reduplication of the zygote from which it sprang, a detached bit of living matter made up largely of certain characteristic protein-complexes. Even the simplest protein is a huge molecule built up of a series of different kinds of amino-acid " nuclei " which in different proteins differ in numbers, kinds and arrangements. Certain of them seem necessary to all proteins, others are present in only some proteins. Each amino-acid, besides being linked to its fellow, has a replaceable hydrogen atom which may be exchanged for any one of several radicals or " side-chains." Furthermore, the ordinary native proteins are secondarily compounded of a number of the simpler blocks formed of linked amino-acids. The unitary amino-acids which enter the blood as protein digestion-products are used as building units again, each cell selecting the kind of units it requires for replacements in its own proteins.

We have no reason to believe that the proteins of the germ-cells have any mysterious powers associated with them that are not shared by any or all of the somatic cells. The modern view of embryogenesis and histogenesis no longer finds it necessary to picture troops of pangenes departing from their home in the nucleus at just the proper time to take possession of the cytoplasm and turn the cell into a specific tissue-cell. Each tissue-cell probably retains all the essential properties of the original fertilized ovum from which it has directly descended. In many cases, among lower organisms, at least, we know that somatic cells detached as buds or experimentally can through regulation and new growth reconstruct themselves into complete organisms. That a particular cell takes on the characteristics of a specific tissue seems to be determined by the special environment in which the cells happen to be placed in the organism.[3]

Exactly how much chemical difference there is between two unlike tissues or between the cells of a particular tissue and the germ-cells is not known. As far as we have any cytological evidence to the contrary the nuclei, at least, of the tissue-cells are not essentially different from the nuclei of the germ-cells. While the various tissues differ very much in appearance, this is mainly the result of the accumulations of intercellular products or of cytoplasmic modifications. And many of the latter may be largely changes in colloidal state rather than fundamental changes in chemical composition. In any event, the new condition is one which has sprung from a cellular chemical constitution similar to that of the original zygote. And if this is true, would not any internal or external agent which could affect particular proteins of the somatic cells be able also to influence the homologous elements in the germ-cells?

Inasmuch as I have already twice reported to this Society on the work[4] of Dr. Smith and myself with fowl-serum immunized to rabbit-lens by means of which, through injections into pregnant rabbits, we succeeded in obtaining defective-eyed young, I shall not again relate the details. The most interesting thing about the experiment was the fact that the eye-defects were transmissible to subsequent generations, and inasmuch as the condition could be passed down through the male line alone it is evident that it is based on changes in the germ-cells.

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[3] *Cf.* Child, "Individuality in Organisms"; also "Origin and Development of the Nervous System."

[4] *Jour. Exp. Zool.*, 31, 2, 1920. AM. NAT., LV, 1921.

In later experiments we obtained similarly defective young by injecting rabbit-lens into pregnant rabbits, although we secured this result only after repeated trials and in the young of but one female. Our belief is that the cytolytic serum not only attacked the newly forming fetal lens, but also its representatives in some of the germ-cells of the fetus. This implies, of course, that there is a sufficient thread of chemical identity between the two to render them both susceptible to the same specific influence.

For such serumal effects to be of significance in evolution, however, the antibody or other factor operative on a given tissue-protein would have to be one that could arise directly in the organism itself. But since it is known that animals will develop anaphylaxis against tissues of their own species, and that a rabbit can be made to build spermatotoxins against its own spermatozoa, it is reasonable to suppose that if an animal's own tissues became displaced, injured or otherwise modified, they might cause the production of antibodies. And these, carried by the circulating fluids of the body into the gonads, would have opportunity to influence such protein-complexes there as were similar to those in the tissues which served as antigens. Nor need the germinal and somatic elements in question be identical in constitution, for it is known that while an antibody against a particular tissue shows its highest degree of specificity only against that tissue, nevertheless, it will also react in some degree with other tissues of the same individual. This phenomenon, termed species-specificity, clearly indicates that there is a broad common basis of chemical identity underlying all the tissues of an organism. It is not unreasonable, then, to believe that there is sufficient chemical identity between the proteins of tissue cells and the related proteins of the germ for both to be influenced by the same agents.

To construct a working hypothesis upon the possibilities before us we might suppose that as long as all tissues are in normal physiological balance no antibody or similar modifying agents are developed. The germ-cells, therefore, maintain the exact constitution they derived from the zygote from which they descended. But with the occurrence of injury, undue stimulation or pronounced change in any part of the body, serological changes would probably be produced in the blood-stream and the germ-cells would then be exposed to possible modifying influences. This would be more likely to happen, of course, if the exposure continued through a long period of time. If the influence were disintegrative or poisonous as the cytolysins or cytotoxins evidently are, then probably degenerative changes would ensue. Such a hypothesis affords, perhaps, a plausible explanation of such deteriorative evolutionary processes as those seen in the formation of vestigial organs. As a concrete illustration, purely hypothetical of course, we may suppose that such a species as the mole in gradually changing to a subterranean existence would meet with frequent injuries to the eyes, and that, as a result of the ensuing inflammatory and suppurative conditions, resorptive influences would be set to work which not only affected the proteins of the eye, but also the related proteins of the germ. Once the degenerative process got to going, it might for a time be based in each new generation upon both the direct chronic irritation to the eye and the parallel changes induced in the germ. Finally, we may suppose that the somatic influence would cease when the eyes became of small size and the eyelids remained permanently sealed, but that the conditions induced in the germ would persist. If such atrophied eyes continued to be resorbed more or less in each generation, however, variation toward still further reduction might continue in the germ. Such a progressive degeneration might possibly be ranked as an instance of regressive orthogenesis.

But what of the progressive aspects of evolution? Can serological reactions be invoked here with any show of reason? One great difficulty in dealing with progressive variation is that we know almost nothing about the chemical and physical factors which underly growth, hypertrophy, hyperplasia, metaplasia, or other changes in somatic tissues due to changed internal relations or to unusual environmental stimuli. If we only knew, for instance, what happens in even as simple a case as when epidermal cells develop into a callous in response to undue pressure or friction, we might have a clue as to how, also, constructive changes might occur in germ-cells; but we have no such knowledge.

Certain types of tissue-overgrowth[5] in which there is increase in the size of the tissue-elements (*hypertrophy*) or in the number of such elements (*hyperplasia*) are interesting in this connection. For example, increased strain in bone leads to increased growth of bony tissue, or excessive exercise leads to overdevelopment of certain muscles. In such cases an increased demand on the nutritive stream caused by unusual katabolism results in a physiological hypertrophy. That is, an excessive synthesis of certain types of proteins is set up. Does the impetus to such extra synthesis extend also to the related, though unstimulated, tissues? I know of no evidence bearing directly on this point, although such phenomena as compensatory overgrowth show that there are influences at work outside the immediate tissue itself which are instrumental in inducing the hypertrophy. For example, if one of a pair of organs (lung, kidney, testicle, thyroid) is lacking or is destroyed, the other enlarges in a short time to the size and functional capacity of the pair combined. There is considerable evidence, particularly in the field of pathology, to show that under ordinary conditions the tissue-elements exert a sort of balanced reciprocal restraint, but disturb this and the whole system is more or less deranged until a new equilibrium is established. Since in compensatory adjustments the compensating organ is generally not in direct connection with the one which is missing or disturbed, it seems probable that the agent which incites the hypertrophy is carried by the blood, although the possible influence of the nervous system must also be reckoned with in higher animals. And if there is such a serum-borne agent in the case of compensatory hypertrophy, may there not also be one in that of the ordinary physiological hypertrophy of the exercised muscle or stressed bone? If so, we must keep our minds open to the possibility that it may also stimulate the germinal prototypes of such proteins to additive functioning. For if we had but a single side-chain in common between a protein of somatic tissue and a protein of the germ, anything that could affect one might well be expected to affect the other.

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[5] *Cf.* any General Pathology.

Again, mechanical stimuli, if not too severe, and various irritative substances in amounts sufficiently small not to be destructive or poisonous to the tissues, may stimulate cells to overgrowth. Very small amounts of arsenic or phosphorus, for example, may thus affect the kidneys and liver, and minute doses of phosphorus may cause increased growth of bone. In such cases also it is probable that serological changes are involved. This is almost certainly true in cases of vicarious overgrowth, where an organ supposedly of related function takes over wholly or in part the work of another tissue. An example of this is seen in the enlargement of the pituitary gland when the thyroid is atrophied or removed, or the compensatory enlargement of the hemolymph glands and bone-marrow following removal of the spleen. Still further may be cited the phenomena of metaplasia, in which, through modification of function and nutrition, specialized tissues develop from cells which normally produce tissue of another order. It sometimes happens, for example, that the choroid coat of a severely injured eye, after the lapse of considerable period of time, will develop a layer of true bone. In fact, metaplastic formation of bone is common in many tissues. Such facts show that many, if not all, tissue-cells have the capacity to form very different kinds of tissue in different environments, and suggest that they retain all the inherencies of the germ. They are what they are somatically because of the special restrictions or excitations of their particular situation in the organism. But if these highly specialized tissue-cells can be so stimulated as to form an entirely different type of tissue, may not such stimulative influences invade even the germ-cell with modifying effects?

Lastly, there are the endocrinal secretions to be reckoned with. Since they are at present popular subjects of research and are constantly being alluded to and discussed in the biological literature of the day, I need not review the field. It is evident that in them we have circulating through the body a series of powerful substances capable of producing profound effects in any or all parts of the body. Through them, apparently, various organs effect reciprocal stimulations and the tissue-complexes of the entire body are maintained in a state of general physiological equilibrium. Both clinical and experimental evidence reveals that hypertrophy or atrophy of an endocrine gland may be followed by marked alterations of structure or function in one or more regions of the body. Thus the cretinism or the myxœdematous condition which results from removal of the thyroid or arrest in its function, or the symptoms resembling exophthalmic goiter following hyperthyroidism are familiar examples. The remarkable overgrowth of the bones of the extremities and head known as acromegaly—morbid giantism—associated with enlargement of the pituitary body is another. Also the relations of the gonads to the secondary sexual characters are well known, as is that of the fetus to the normal hypertrophy of the mammary glands in pregnancy.

Since hypertrophy or atrophy of an endocrine may produce deep-seated permanent changes in various tissues of an organism, I would again point out the possibility that the germinal homologues of the proteins of such tissues, if such there be, might likewise be permanently modified, and that if for some reason there came a constant inherited increase or diminution of an endocrine gland, or an environmental modification of it generation after generation, we might have in its waxing or waning output the excitant necessary for germinal changes which become outwardly expressed as a series of orthogenetic changes. That this suggestion of endocrinal influence on the germ is not so far fetched as would appear at first sight, is evident, I think, when we recall that certain of the conditions which can be induced in individuals by experimental or pathological endocrinal upsets are known to occur also as congenital defects which are inheritable. For example, short-fingeredness (brachydactyly) may be induced after birth by too much pituitary secretion, but such a condition is also well known as a congenital defect which is hereditary. In the latter case, is it more reasonable to suppose that the short-fingeredness, could we trace it back into the germ, is really represented by a factor that has to do primarily with the finger or with a factor directly concerned in some way with the pituitary body? And did hypertrophy of the pituitary body originally induce the heritable type of brachydactyly? We do not know, but the parallelism of the two conditions, it seems to me is highly suggestive.

And let us glance for a minute at one of the well-known studies on orthogenesis; that of Ruthven[6] on the variations of scutellation in the garter snakes. In his own words:

> . . . it seems to me that the most tenable hypothesis of the evolution of the genus *Thamnophis* is that it originated and became differentiated into four main groups in northern Mexico. From this region the groups radiated in all directions, but principally to the northward, and wherever they entered different regions the changed environmental conditions acted as an unfavorable stimulus which retarded growth, and differentiated the groups into dwarfed forms.

And in another place he generalizes as follows:

> (1) That the maximum scutellation and size in the genus *Thamnophis* occurs in the center of dispersal, and the forms that have been produced in the history of its migration have been formed principally by dwarfing and by a reduction in scutellation; (2) that the variation in the number of scales in the different series is

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[6] Bull. 61, U. S. Nat. Mus., 1908.

definite and not promiscuous, and is correlated in a remarkable degree with changes in the environment.

Have we not here a condition strikingly like what we should expect to find if some factor or factors, external or internal, were operating in such a way as to lessen the output of some endocrinal secretion concerned in growth or the determination of size? This is at least a possibility worthy of consideration.

In closing may I say that in what I have put before you I do not pretend to have supplied the established facts necessary for founding a scientific theory. The discussion is largely a series of suggestions, a mere working scheme which takes into account various phenomena that appear to be related, and which in their present states of disclosure seem to lend themselves to some such interpretation as I have tried to give. It is presented because, in my estimation, it suggests a line of thought we may well entertain when we are wrestling with our several problems of genetics, variation and evolution. For if it can be clearly established that any one of the serological influences can reach specifically from soma to germ then it becomes a plausible hypothesis that many of them do. If a changed or changing external or internal environment causes a long continued physiological stress of certain parts, then as long as this stress is accompanied by changed conditions of the circulating fluids of the body, so long also will the germ-cells be exposed to these influences. If they are such as to induce variations in definite directions, orthogenesis must be the outcome.

And if serological influences play an important part in adaptive somatic changes, such as adaptive hypertrophies—or for that matter, adaptive atrophies—then we have the way open to conceive of how adaptive germinal changes may likewise be the outcome of these same influences.

It is a noteworthy fact that in the geological past whenever conditions suitable for new types of existence occurred, new forms of life well adapted to the conditions appeared. This has happened not only once, but repeatedly. And since satisfactory adjustment to the new conditions must mean not only one, but many favorable and interrelated variations, it seems almost incredible that the adaptedness characteristic of the organisms in question was attained merely through the operation of natural selection generation after generation on assemblages of purely accidental mutations. Palæontologists tell us that times of marked evolutionary change have coincided with periods of great geological change—extremes of temperature, moisture or drought, or fairly rapid fluctuation between such extremes. And while such conditions would undoubtedly favor a maximal operation of natural selection, it is well to remember also that the severe strains of somatic adjustment forced upon organisms existing at the time would doubtless result in a maximal sweep of serological influences through the sorely pressed body.

Although I have emphasized one side of the problem of variation, I am not unmindful of the remarkable stability of the germinal protoplasm as we see it expressed in organisms to-day. It is obvious that not every minor or temporary alteration in somatic mechanism is reflected in the germ to any measurable extent. Since probably no two living things of any kind are equally susceptible to external influence, individual germ-cells doubtless vary in susceptibility, possibly even the same germ-cell would respond differently at different stages of maturity. It is not unreasonable to believe, moreover, that only a few out of many germ-cells might be sufficiently affected to make a perceptible difference. I have already expressed the opinion[7] elsewhere that "no one to-day, qualified by his knowledge of embryology and genetics to the right of an opinion, would, I think, deny that the new organism is in the main the expression of what was in the germ-line, rather than of what it got directly from the body . . . ." But we know that the germ does change from time to time and it seems to my mind not illogical to suppose that at least some of the changes are specifically related to changes in the soma.

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[7] AM. NAT., LV, Mar.-Apr., 1921.